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10/631,106	07/31/2003	Dennis M. Brown	067716-5003-US02	7746

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EXAMINER	
ROYDS, LESLIE A	
ART UNIT	**PAPER NUMBER**
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/631,106	BROWN, DENNIS M.	
	Examiner	Art Unit	
	Leslie A. Royds	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 May 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *15-19 and 22-26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *15-19,22-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 15-19 and 22-26 are presented for examination.

Applicant's Amendment filed May 7, 2008 has been received and entered into the present application.

Claims 15-19 and 22-26 remain pending and under examination. Claims 27-30 are cancelled.

Applicant's arguments, filed May 7, 2008, have been fully considered. Rejections not reiterated from previous Office Actions are hereby withdrawn. The following rejections are either reiterated or newly applied. They constitute the complete set of rejections presently being applied to the instant application.

Claim Rejections - 35 USC § 112, First Paragraph, Scope of Enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 15-19 and 22-26 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the use of amonafide in conjunction with homoharringtonine for the treatment of fibrosarcoma, does not reasonably provide enablement for the treatment of solid tumors generally with the combination of amonafide with homoharringtonine, for the reasons already made of record at pages 6-11 of the previous Office Action dated November 7, 2007, of which said reasons are herein incorporated by reference.

Applicant traverses the instant rejection, stating that the test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation. Applicant relies upon the references to Mattern et al., Geran et al. and Welch to establish that the use of transplanted tumor models to determine

the efficacy of various potential chemotherapeutic compounds against a host of different types of tumors was well-established in the art as of the time of the invention. Applicant alleges that the cited literature demonstrates that numerous models existed for testing the effectiveness of various compounds against a variety of different tumors, and these models were recognized as being useful for identifying activity against disease. Applicant asserts that the wealth of knowledge that existed in the art at the time of the invention would have allowed the artisan to determine whether the combination of homoharringtonine and amonafide was effective in exerting an anticancer effect against a wide range of tumors.

Applicant's traversal has been fully and carefully considered, but fails to be persuasive.

Firstly, the issue at hand is not whether it was known in the art how to use transplanted tumor models to determine the efficacy of a potential chemotherapeutic compound against various tumor types but rather whether, given the unpredictability in the art at the time of the invention, the skilled artisan would have been imbued with at least a reasonable expectation of success in treating *any* solid tumor with a combination of amonafide and homoharringtonine based on the guidance and direction provided in the present specification. Though the art may very well recognize the ability to use transplanted tumor models of different cancers to determine the activity of a potential chemotherapeutic agent in treating such cancers, this does not change the fact that Applicant has exemplified amonafide in combination with homoharringtonine for the treatment of only one type of solid tumor in the instant specification and fails to clearly address the high degree of variability in the art with regard to the pathophysiological differences among all solid tumor types and their reactivity to different anticancer agents, particularly when combined for adjuvant therapy, such that the activity seen with a single agent in a single cancer would not necessarily be predictive of the same or similar level of activity in any other cancer type given the state of the art.

While Applicant's reliance upon the references to Mattern et al., Geran et al. and Welch establishes that a potential chemotherapeutic compound may be tested in various transplanted tumor

models to determine its activity in treating that discrete tumor type, the citation of such references fails to speak to, or address even tangentially, the issue of unpredictability in the art with regard to the treatment of cancer. As previously set forth on the record (see, e.g., p.5 of the Office Action dated September 25, 2006), the state of the art was such at the time of the invention that it (1) failed to recognize the ability to effectively treat cancerous conditions due to the challenging and complex nature of neoplasia in general and (2) also failed to recognize the ability to use a single agent for the generic treatment of any cancer or neoplastic condition or solid tumor. This is clearly supported by the reference to Cecil's Textbook of Medicine as discussed at pages 9-16 of the previous Office Action dated March 24, 2006. Furthermore, given that the art was aware of three distinctly different types of solid tumors [(1) sarcomas, those that arise from connective or supporting tissues, such as bone or muscle, (2) carcinomas, those that arise from glandular tissues and epithelial cells, and (3) lymphomas, those that arise from the lymphoid organs, such as the lymph nodes, spleen or thymus], the distinct etiology and pathophysiological differences between these three categories of solid tumors would not have imbued the skilled artisan with a reasonable expectation of success in treating any one or more of these types of solid tumor when efficacy had only been demonstrated in a sarcoma (i.e., fibrosarcoma) murine model, given this unpredictability inherent in the cancer art.

Applicant once again has conspicuously failed to address the asserted unpredictability inherent in the cancer art by providing evidence in the form of data, publications supporting the state of the art at the time of the invention or scientifically persuasive reasoning to support the conclusion that this single example in a single solid tumor type would have been predictive of the same or at least similar level of efficacy over the full breadth of subject matter presently claimed. Though Applicant does cite publications supporting the use of transplanted tumor models to determine the activity of a potential chemotherapeutic agent, such documents again fail to establish any degree of predictability in the cancer art such that one of skill in the art would have understood that the single example provided in the

specification would have been reasonably suggestive of similar efficacy over the full scope of claimed subject matter. As a result, it remains that the instant specification lacks sufficient guidance or direction as to how one of skill in the art would be able to determine what other solid tumors aside from fibrosarcoma would be reasonably effectively treated using the instantly claimed combination of agents without have to undertake extensive hit or miss testing that would clearly rise to the level of undue experimentation for the reasons already made of record.

Furthermore, though Applicant has repeatedly alleged on the record that the skilled artisan would have understood that the results obtained in the fibrosarcoma cell model would have been understandably predictive of similar results in other tumor systems, as well as predictive of the same efficacy in any type of solid tumor, it remains that the art overwhelmingly speaks to the contrary of this conclusion by clearly teaching that such objectives as instantly claimed by Applicant have never been achieved in the art. As a result, the idea that the efficacy seen in this single cell model would correlate to clinical success of the same degree in any solid tumor is clearly unsupported by the art at the time of the invention due to the pathophysiologic, histological and etiologic variation in solid tumor types and the fact that various tumors exhibit highly variable therapeutic responses to the same type of therapy. Accordingly, Applicant's opinion that the single cell model exemplified in the instant specification would be indicative of the same efficacy in any type of solid tumor in the absence of any evidence and/or scientific reasoning in support of this extrapolation is, once again, as before, no more than an allegation without factual support, which is unpersuasive.

In view of the foregoing, when all of the evidence is considered, the totality of rebuttal evidence of enablement fails to outweigh the evidence in support of the instant conclusion of a lack of adequate enabling guidance presented in the instant specification.

For these reasons presented *supra*, and those previously made of record at pages 6-11 of the Office Action dated November 7, 2007, the claims remain properly rejected under 35 U.S.C. 112, first paragraph, and the rejection is **maintained**.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 15-19 and 22-26 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Scheithauer et al. ("Phase II Study of Amonafide in Advanced Breast Cancer", *Breast Cancer Research and Therapeutics*, 20:63-67; 1991) in view of Jiang et al. ("Comparative *In Vitro* Antitumor Activity of Homoharringtonine and Harringtonine Against Clonogenic Human Tumor Cells", *Investigational New Drugs*, 1:21-25; 1983), each already of record, for the reasons of record set forth at pages 12-16 of the previous Office Action dated November 7, 2007, of which said reasons are herein incorporated by reference.

Applicant traverses the instant rejection, stating that Table 5 of the instant specification shows that the combination of amonafide and homoharringtonine is more effective than either amonafide and homoharringtonine administered alone. Additionally, Applicant argues against the application of *Kerkhoven* because the case involved a combination of detergents and the combination of two anticancer agents results in less obvious effects on a patient than the effect of combining two detergents to form a third detergent. Still further, Applicant alleges that the cases of *Kerkhoven, Susi, Crockett, Linder* and *Dial* are not analogous to the present situation and, therefore, the presumptions therein regarding the obviousness of combinations due to predictable effects do not apply. Lastly, Applicant argues that

Scheithauer teaches against using amonafide in combination with other cancer therapies because the reference teaches that the response rate of patients was found to be higher in those patients without prior anthracycline exposure. Applicant cites to the references to Reitemeier et al. and Norris et al. in support of the assumption that combinations of cancer drugs do not necessarily result in additive effects.

Applicant's traversal has been fully and carefully considered, but fails to be persuasive.

Firstly, though Applicant urges unexpected results of the instantly claimed combination of amonafide and homoharringtonine as evidence of non-obviousness and references the data presented in Table 5 of the instant specification, Applicant's assessment of the data conspicuously fails to take into account that the measurement of tumor volume quadrupling time (TVQT) for amonafide (50 mg/kg) is 9.7 ± 0.6, homoharringtonine (4 mg/kg) is 8.5 ± 0.5 and the combination of amonafide (30 mg/kg) and homoharringtonine (4 mg/kg) is 10.2 ± 0.5, which is clearly within the standard deviation of error measured for the TVQT of amonafide alone. In other words, amonafide (50 mg/kg) produced a TVQT of 9.7 ± 0.6, which clearly covers a range of 9.1 to 10.3 and, thus, clearly encompasses the same TVQT measured for the combination of amonafide and homoharringtonine. Moreover, Applicant has failed to make a comparison of a combination of amonafide and homoharringtonine in the same concentrations used to measure TVQT of each agent separately. Accordingly, the combination of amonafide and homoharringtonine using an amount of amonafide that differs from that used when TVQT was measured following amonafide administration alone would have been *reasonably expected* to result in a difference in TVQT value and, thus, fails to support Applicant's instant allegation that the results seen using the exemplified combination of amonafide and homoharringtonine are, in fact, unexpected.

Moreover, even if, *arguendo*, the data did support an unexpected effect (which the Examiner does not concede), the proffered results do not provide a basis for concluding that the full scope of the claimed subject matter would not have been obvious because the results are limited to specific dosage amounts (i.e., 30 mg/kg amonafide and 4 mg/kg homoharringtonine) and the use of the compounds in what appears

to be simultaneous administration, while the instant claims subject to this rejection encompass the use of amonafide and homoharringtonine in *any amounts that provides an anticancer effect and further in any type of "combination"* (i.e., simultaneously; separately with amonafide administered prior to homoharringtonine or vice versa, etc.). Further, it has not been argued or demonstrated on the record that the results obtained with the exemplified combination(s) would have been exemplary of the same or substantially similar results that would have been expected to occur over the wide range of possible therapeutic amounts that provide an anticancer amount or types of combination therapy encompassed by the present claims.

In this regard, MPEP §2144.08(II)(B) is relied upon and reads, in-part: "When considering whether proffered evidence is commensurate in scope with the claimed invention, Office personnel should not require the Applicant to show unexpected results over the entire range of properties possessed by a chemical compound or composition. See, e.g., *In re Chupp*, 816 F.2d 643, 646, 2 USPQ2d 1437, 1439 (Fed. Cir. 1987). Evidence that the compound or composition possesses superior and unexpected properties in one of a spectrum of common properties can be sufficient to rebut a *prima facie* case of obviousness. Id. For example, a showing of unexpected results for a single member of a claimed subgenus, or a narrow portion of a claimed range would be sufficient to rebut a *prima facie* case of obviousness if a skilled artisan 'could ascertain a trend in the exemplified data that would allow him to reasonably extend the probative value thereof.' *In re Clemens*, 622 F.2d 1029, 1036, 206 USPQ 289, 296 (CCPA 1980) (**Evidence of the unobviousness of a broad range can be proven by a narrower range when one skilled in the art could ascertain a trend that would allow him to reasonably extend the probative value thereof.**) But see, *In re Grasselli*, 713 F.2d at 743, 218 USPQ at 778 (Evidence of superior properties for sodium containing composition insufficient to establish the non-obviousness of broad claims for a catalyst with 'an alkali metal' where it was well known in the catalyst art that different alkali metals were not interchangeable and Applicant had shown unexpected results only for sodium

containing materials); *In re Greenfield*, 571 F.2d 1185, 1189, 197 USPQ 227, 230 (CCPA 1978) (Evidence of superior properties in one species insufficient to establish the nonobviousness of a subgenus containing hundreds of compounds); *In re Lindner*, 457 F.2d 506, 508, 173 USPQ 356, 358 (CCPA 1972) (one test not sufficient where there was no adequate basis for concluding the other claimed compounds would behave the same way)." (emphasis added)

Here, even though the results shown with a single formulation comprising 30 mg/kg amonafide and 4 mg/kg homoharringtonine administered apparently simultaneously demonstrated results in prolonging TVQT that were both unexpected and unpredictable from the prior art, just as a single point in space fails to define a line, the results demonstrated for this discrete combination is insufficient to establish the non-obviousness of the entirety of the presently claimed subject matter [i.e., any amounts that provides an anticancer effect and further in any type of "combination" (such as, e.g., simultaneously; separately, wherein amonafide is administered prior to homoharringtonine or vice versa, etc.)] absent any concrete evidence or scientifically sound reasoning as to why (1) any other dosage amounts over the wide range of possible dosage amounts that would provide an anticancer effect and (2) why separate/sequential and/or non-simultaneous administration would have been reasonably expected to demonstrate the same synergistic effect in extending TVQT.

Accordingly, while Applicant's remarks and data provided in Table 5 have been fully and carefully considered, it remains that Applicant has not provided sufficient evidence and/or explanation to support the allegation that a synergistic effect in extending TVQT using the claimed combination of amonafide and homoharringtonine has been demonstrated over the full scope of the claimed subject matter. Furthermore, Applicant has failed to provide any objective evidence, scientific reasoning or persuasive argument on the record to provide an adequate basis for concluding that the discrete combination exemplified is probative of the same (or at least substantially similar) synergistic effect over the entire scope of the claimed invention. In short, the evidence is, respectfully, insufficient to be

supportive of nonobviousness on the basis of a synergistic result over the full scope of the claimed subject matter because the proffered data is not commensurate in scope with the claimed subject matter.

Secondly, Applicant argues against the application of *In re Kerkhoven* to support the *prima facie* obviousness of combining two or more components, each with the same utility, because Applicant asserts that *Kerkhoven* was directed to a combination of detergents, which is much less complicated than a combination of two anticancer drugs. Though it is noted that *Kerkhoven* was decided within the factual context of combining detergents, this fact alone does not, without more, preclude the extension of this reasoning to pharmacological agents or chemical compounds in general. *Kerkhoven* supports the overall *concept* of combining equivalents known for the same purpose and is logically extended to equivalents for any known purpose, be it detergents or, as in the present case, anticancer compounds, with the *reasonable expectation* that the two agents, when combined, would produce at least additive (if not synergistic) effects when combined. See MPEP §2144.06. In addition, the artisan skilled in the pharmaceutical and medical arts would have reasonably been aware of, and clearly recognized the complexity inherent in these arts and would have proceeded accordingly when making such a combination.

Thirdly, Applicant's argument that Scheithauer teaches away from using amonafide in combination with other cancer therapies because the reference teaches that the response rate of patients was found to be higher in those patients without prior anthracycline exposure is unpersuasive. Scheithauer et al. *explicitly and unequivocally* provides a motivation to combine amonafide with other chemotherapeutic agents. Please see p.67, col.1, last paragraph of Scheithauer et al., which teaches, "In summary, our results suggest that amonafide is an active agent in the treatment of patients with advanced breast cancer. ***The drug should therefore be considered for further evaluation and incorporation in combination chemotherapy***." Accordingly, in view of such a teaching, it is very clear that Scheithauer et al. provides an express direction *to combine amonafide* with another chemotherapeutic agent, and does

not, as alleged by Applicant teach away from its use with other chemotherapeutics. Note also that the patients that Applicant relies upon to allege a teaching away are those that have been *previously exposed to anthracycline*, not those that have been concomitantly exposed to anthracycline (i.e., a combination therapy as instantly claimed) and, therefore, is clearly not directed in any way to a teaching away from combination chemotherapeutic regimens.

Fourthly, and lastly, Applicant's reliance upon the references to Reitemeier et al. and Norris et al. in support of the assumption that combinations of cancer drugs do not necessarily result in additive effects is also unpersuasive because the agents cited in the references that are used in combination are distinctly different in structure, function and effect/mechanism of action from the two agents instantly claimed (i.e., amonafide and homoharringtonine) such that the efficacy seen using combinations of the agents of the cited references (i.e., doxorubicin, vinorelbine, 5-FU, mitomycin C, BCNU, etc.) would not have been reasonably predictive of the same efficacy (or lack thereof) when used in combination, absent any factual evidence or scientific reasoning to support the extrapolation of the effects seen with these anticancer combinations to other combinations of anticancer agents, particularly the two agents instantly claimed.

Furthermore, Applicant is requested to clarify his position regarding the predictability of efficacy of anticancer agents. Applicant appears to be of the position that the effects of anticancer agents are not as predictable as, e.g., detergent compounds, (see, e.g., p.7 of the Remarks filed May 7, 2008), but clearly contradicts this position by now alleging that the efficacy observed using combinations of distinctly different anticancer agents can be predictably extrapolated to the instantly claimed combination of amonafide and homoharringtonine to support the assumption that the skilled artisan would not have expected the instantly claimed combination (asserted to be an obvious combination from the prior art) to result in at least an additive effect. Accordingly, clarification is requested.

For these reasons presented *supra*, and those previously made of record at pages 12-16 of the previous Office Action dated November 7, 2007, rejection of claims 15-19 and 22-26 remains proper and is **maintained**.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., In re Berg, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); In re Van Ornum, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); In re Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In re Thorington, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 15-19, 22-24 and 26 remain provisionally rejected on the grounds of nonstatutory obviousness-type double patenting as being unpatentable over claims 50-52 and 58-59 of U.S. Patent Application No. 10/976,961 in view of Scheithauer et al. ("Phase II Study of Amonafide in Advanced Breast Cancer", *Breast Cancer Research and Therapeutics*, 20:63-67; 1991) and Jiang et al. ("Comparative *In Vitro* Antitumor Activity of Homoharringtonine and Harringtonine Against Clonogenic Human Tumor Cells", *Investigational New Drugs*, 1:21-25; 1983), each already of record, for the reasons of record set forth at pages 17-19 of the previous Office Action dated November 7, 2007, of which said reasons are herein incorporated by reference.

Cancellation of claims 27-30 renders the instant rejection **moot** as applied to such claims.

Applicant requests that the instant rejection be held in abeyance until claims from the cited application have issued or until the double patenting rejection is the only rejection that remains.

In view of the fact that none of the claims in the cited application have issued and further that the instant double patenting rejection is not the only rejection that remains in the instant case, the present provisional rejection remains proper and is **maintained**.

Claim 25 remains provisionally rejected on the grounds of nonstatutory obviousness-type double patenting as being unpatentable over claims 42-44 of U.S. Patent Application No. 10/976,961 in view of Scheithauer et al. ("Phase II Study of Amonafide in Advanced Breast Cancer", *Breast Cancer Research and Therapeutics*, 20:63-67; 1991) and Jiang et al. ("Comparative *In Vitro* Antitumor Activity of Homoharringtonine and Harringtonine Against Clonogenic Human Tumor Cells", *Investigational New Drugs*, 1:21-25; 1983), each already of record, for the reasons of record set forth at pages 20-21 of the previous Office Action dated November 7, 2007, of which said reasons are herein incorporated by reference.

Applicant requests that the instant rejection be held in abeyance until claims from the cited application have issued or until the double patenting rejection is the only rejection that remains.

In view of the fact that none of the claims in the cited application have issued and further that the instant double patenting rejection is not the only rejection that remains in the instant case, the present provisional rejection remains proper and is **maintained**.

Claims 15-19 and 22-26 remain provisionally rejected on the grounds of nonstatutory obviousness-type double patenting as being unpatentable over claims 1 and 10-16 of U.S. Patent Application No. 11/676,176 in view of Scheithauer et al. ("Phase II Study of Amonafide in Advanced Breast Cancer", *Breast Cancer Research and Therapeutics*, 20:63-67; 1991) and Jiang et al. ("Comparative *In Vitro* Antitumor Activity of Homoharringtonine and Harringtonine Against Clonogenic Human Tumor Cells", *Investigational New Drugs*, 1:21-25; 1983), each already of record, for the reasons

of record set forth at pages 21-23 of the previous Office Action dated November 7, 2007, of which said reasons are herein incorporated by reference.

Cancellation of claims 27-30 renders the instant rejection **moot** as applied to such claims.

Applicant requests that the instant rejection be held in abeyance until claims from the cited application have issued or until the double patenting rejection is the only rejection that remains.

In view of the fact that none of the claims in the cited application have issued and further that the instant double patenting rejection is not the only rejection that remains in the instant case, the present provisional rejection remains proper and is **maintained**.

Conclusion

Rejection of claims 15-19 and 22-26 remains proper and is **maintained**.

No claims of the present application are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leslie A. Royds whose telephone number is (571)-272-6096. The examiner can normally be reached on Monday-Friday (9:00 AM-5:30 PM).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin H. Marschel can be reached on (571)-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Leslie A. Royds/
Patent Examiner, Art Unit 1614

August 13, 2008

/Ardin Marschel/
Supervisory Patent Examiner, Art Unit 1614